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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,342	07/27/2000	DAVID J. CLARKE	39-206	8022

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EXAMINER	
YANG, NELSON C	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 12/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/529,342	CLARKE ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's cancellation of claims 1-41 is acknowledged and has been entered.

2. Applicant's addition of claims 42-61 is acknowledged and has been entered.

3. Claims 42-61 are currently pending.

Rejections Withdrawn

4. Applicant's arguments, see page 7, filed May 20, 2004, with respect to the objection to the specification have been fully considered and are persuasive. The objection of the specification has been withdrawn.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 42-49, 51, 53, 54, 58, 61 are rejected under 35 U.S.C. 102(e) as being anticipated by Cullis et al [US 6,417,326].

With respect to claim 42, Cullis et al teach the use of fusogenic liposomes containing fusogenic lipopeptides (column 16, lines 25-30), including GALA (column 17, lines 42-43). Cullis et al specifically teach that pH-sensitive fusogenic polymers which can be incorporated into or covalently attached to liposome vesicles. These pH-

sensitive fusogenic polymers trigger fusion or release of the contents of the carrier systems on protonation of the carboxyl groups when the carrier systems encounter an acidic environment (column 25, lines 1-26), which are sometimes found in tumors (column 31, lines 44-45). Cullis et al teach targeting mechanisms such as monoclonal antibodies specific to antigens associated with neoplasms (column 28, lines 44-50) and require that the targeting agents be positioned on the surface of the liposome in such a manner that the target moieties are available for interaction with the target such as a cell surface receptor (column 29, lines 4-10). Cullis et al further teach the use of a fluorescent marker ANTS for determining the pH-induced destabilization of membranes (column 59, lines 5-20).

7. With respect to claims 43-45, Cullis et al teach that the lipopeptide is incorporated into the outer monolayer of a liposome, or alternatively, into both the inner and outer monolayers of a liposome (column 16, lines 25-33).

8. With respect to claims 46-48, Cullis et al teach targeting mechanisms such as monoclonal antibodies specific to antigens associated with neoplasms (column 28, lines 44-50) and require that the targeting agents be positioned on the surface of the liposome in such a manner that the target moieties are available for interaction with the target such as a cell surface receptor (column 29, lines 4-10), and comprise a connector portion which must have both a lipophilic anchor and a hydrophilic reactive group suitable for reacting with the target agents (column 29, lines 15-20).

9. With respect to claim 49, Cullis et al demonstrates that the liposomes form aggregates (column 44, lines 5-10).

10. With respect to claims 51-53, Cullis et al teach the use of fusogenic liposomes containing fusogenic lipopeptides (column 16, lines 25-30), including GALA (column 17, lines 42-43) and melittin (column 15, lines 34-35).

11. With respect to claim 54, Cullis et al further teach the use of a fluorescent marker ANTS for determining the pH-induced destabilization of membranes (column 59, lines 5-20).

12. With respect to claims 58, 61, Cullis et al teach targeting mechanisms such as monoclonal antibodies specific to antigens associated with neoplasms (column 28, lines 44-50).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claim 50 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cullis et al [US 6,417,626] in view of Li et al [US 5,512,294].

Cullis et al teach the use of targeting agents, as discussed above. Cullis et al do not teach the use of targeting agents comprising a first binding moiety comprising avidin or a derivative of avidin and a second binding moiety comprising biotin or a derivative of biotin.

Li et al, however, teach liposomes where antibodies may be attached by the biotin-avidin biotinylated antibody sandwich (fig.16, column 9, lines 65-67), in order to

allow a variety of commercially available biotinylated antibodies to be used on the polymerized liposome particles (column 10, lines 1-3).

Therefore, it would have been obvious to attach antibodies by a biotin-avidin biotinylated antibody sandwich, as suggested by Li et al, onto the liposomes in the method of Cullis et al, in order to be able to allow a variety of commercially available biotinylated antibodies to be used on the polymerized liposome particles.

15. Claims 55-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cullis et al [US 6,417,326] in view of Levinson et al [US 6,020,142].

Cullis et al teach a method comprising the steps of treating a sample with lipid vesicle particles incorporating a cytolytic peptide such as GALA that modulates the permeability of the particles in response to a predetermined metabolic signal from a targeted cell type as discussed above. Cullis et al do not teach that the species is an enzyme or a substrate for an enzyme.

Levinson et al, however, teach the use of a delivery complex such as liposomes (column 3, lines 5-12) for delivering enzymes and substrates such as glucose oxidase (column 25, lines 40-42) in order to label RATH gene peptide-specific antibodies. This is important as the RATH1.1 gene product has been demonstrated to act as a mediator of signal transduction events, and and the detection of compounds which modulate the RATH gene product would allow for the diagnostic evaluation, prognosis, and treatment of immune disorders involving T cell activation (column 1, lines 29-62).

Therefore it would have been obvious in the method of Cullis et al to have the liposomes deliver enzymes and substrates such as glucose oxidase, as suggested by

Levinson et al, in order to allow for the diagnostic evaluation, prognosis, and treatment of immune disorders involving T cell activation.

16. Claim 59 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cullis et al [US 6,417,326] in view of Robinson et al [US 5,994,149].

Cullis et al teach the use of lipid particles to detect pathogenic cells, as discussed above. Cullis et al do not teach the detection of pathogenic cells in foodstuffs.

Robinson et al, however, do teach the analysis of foodstuffs for pathogenic cells using liposomes (column 4, lines 19-24). Robinson et al further teach that it would be desirable to have a test kit that would eliminate operator error, and have a predictably accurate and reproducible rate of identification of pathogenic fungi, yeasts and molds (column 1, lines 16-45).

Therefore it would be obvious to teach the detection of pathogenic cells in foodstuffs, as taught by Robinson et al, in the method of Cullis et al, in order to have a test kit that would eliminate operator error, and have a predictably accurate and reproducible rate of identification of pathogenic fungi, yeasts and molds.

17. Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cullis [US 6,417,326] in view of Blondin et al [US 4,808,517].

Cullis et al teach the use of lipid particles to detect pathogenic cells, as discussed above. Cullis et al do not teach the detection of pathogenic cells in water samples.

Blondin et al, however, do teach a method of using of lipid vesicles (column 4, lines 9-24) for the detection of toxins in water samples (column 8, lines 20-32) that is

economical and efficient and can be quickly and easily performed (column 2, lines 64-68).

Therefore it would be obvious to use the method of Cullis et al to analyze water samples for pathogens as taught by Blondin et al, in order to detect toxins economically, efficiently, quickly and easily.

Response to Arguments

18. Applicant's arguments with respect to claims 1-17 have been considered but are moot in view of applicant's cancellation of claims 1-41 and in view of the new ground(s) of rejection.

Conclusion

19. No claims are allowed.

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

21. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the

advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

22. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

23. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nelson Yang
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Art Unit 1641

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11/24/04